

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Yurgelun-Todd et al.	Confirmation No.:	5991
Serial No.:	10/556,134	Art Unit:	1651
§ 371 Date:	February 12, 2007	Examiner:	Aaron J. Kosar
Customer No.:	21559		
Title:	USE OF SECRETIN IN TREATMENTS OF DISORDERS ASSOCIATED WITH THE AMYGDALA		

DECLARATION UNDER 37 C.F.R. § 1.131 OF PRIOR INVENTION

Under 37 C.F.R. § 1.131, we declare:

1. We are the inventors of the subject matter that is described and claimed in the above-captioned patent application.
2. The enclosed Exhibit is a copy of an invention disclosure, which shows that we had conceived the invention of the relevant claims prior to March 13, 2003. In particular, these pages show conception of the use of secretin for the treatment of bipolar disorder and other psychiatric disorders. The invention was conceived in the U.S.
3. As is stated in the Exhibit, we believed that the effects of secretin may be mediated, in part, by its effects on the amygdala. We further employed fMRI in the study of adolescents with bipolar disorder and observed abnormalities in the amygdala of these subjects.
4. We diligently worked to reduce the invention to practice from just prior to March 13, 2003 to May 13, 2003, the filing date of the provisional application from which this application claims priority.

Diligence is evidenced by our work on an NIMH grant proposal to obtain federal funding to conduct studies of facial affect in patients with bipolar disorder during February - March 2003. In addition, between February and April, 2003, we developed a protocol to study masked vs. unmasked facial affect using fMRI. These experiments are relevant as bipolar subjects demonstrate altered amygdalar activation during facial affect tasks, and secretin modifies amygdalar activation during facial affect task.

From February to May 2003, we worked to demonstrate prefrontal cortex modulation of amygdalar activation in bipolar disorder. From March 2003 through May 13, 2003, we developed methods to increase the ability of fMRI to determine the effects of secretin on the central nervous system. From April to May 2003, we developed a protocol to assess the effects of secretin on brain activation in patients with schizophrenia. These activities are relevant to the invention because we believe that secretin produces a therapeutic effect at least in part through effects on the amygdala, and these studies sought to confirm a connection between bipolar disorder and schizophrenia and abnormalities of the amygdala.

These tasks were also carried out in the U.S.

5. All statements made herein of our own knowledge are true and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

10/15/2010  
Date

11/18/10  
Date

Deborah A. Yurgeldn-Todd  
Deborah A. Yurgeldn-Todd

Perry F. Renshaw  
Perry F. Renshaw

# EXHIBIT

## THE McLEAN HOSPITAL CORPORATION INVENTION DISCLOSURE FORM

### 1. TITLE OF THE INVENTION.

SECRETIN AS A TREATMENT FOR BIPOLAR DISORDER

2. DESCRIBE THE INVENTION BRIEFLY. (If possible, attach a manuscript, a drawing, an abstract, or any other materials that would assist in the understanding of the invention. Point out novel features, advantages over other methods, and commercial possibilities. Attach additional sheets, if necessary.)

SECRETIN IS A GASTROINTESTINAL HORMONE WHICH MAY BE AN EFFECTIVE TREATMENT FOR AUTISM. AUTISM IS A DEVELOPMENTAL DISORDER CHARACTERIZED BY IMPAIRED SOCIAL INTERACTION. THE EFFECTS OF SECRETIN

3. INVENTORS. (All individuals who qualify as inventors should be listed below. The individual who is named in (1) below is designated as the primary contact for additional information and for all correspondence.)

- (1) Name PERRY RUSMAN Degree M.D., M.D. (over)  
Title \_\_\_\_\_ Dept. \_\_\_\_\_  
Social Security Number \_\_\_\_\_  
Work Address BRAIN IMAGING CENTER, McLENN HOSP.  
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- (2) Name DEBORAH YURETZKY-TEOD Degree Ph.D.  
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Title \_\_\_\_\_ Dept. \_\_\_\_\_  
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- (4) Name \_\_\_\_\_ Degree \_\_\_\_\_  
Title \_\_\_\_\_ Dept. \_\_\_\_\_  
Social Security Number \_\_\_\_\_  
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e-mail \_\_\_\_\_
- (5) Name \_\_\_\_\_ Degree \_\_\_\_\_  
Title \_\_\_\_\_ Dept. \_\_\_\_\_  
Social Security Number \_\_\_\_\_  
Work Address \_\_\_\_\_  
Work Phone \_\_\_\_\_ Fax \_\_\_\_\_  
e-mail \_\_\_\_\_

MAY BE MEDIATED, IN PART, THROUGH ITS EFFECTS ON THE AMYGDALA.

BIPOLAR DISORDER IS A CIRCUIT DISORDER CHARACTERIZED BY PERIODS OF MANIA AND DEPRESSION. HOWEVER, INAPPROPRIATE SOCIAL INTERACTIONS ARE OFTEN A CHARACTERISTIC, POSSIBLY REFLECTING POOR RECOGNITION OF AFFECT AND/OR LIMITED INSIGHT. RECENT STRUCTURAL AND FUNCTIONAL IMAGING STUDIES PERFORMED AT MCGLENN HOSPITAL HAVE IDENTIFIED 9 AMYGDALAR ~~THE~~ ABNORMALITIES IN YOUNG ADULTS WITH BIPOLAR DISORDER.

WE PROPOSE THAT SECREPIN MAY BE OF BENEFIT FOR THE TREATMENT OF BIPOLAR DISORDER, AS WELL AS OTHER AFFECTIVE (E.G. DEPRESSION, CYCLOTHYMIA, ETC.) AND PSYCHOTIC (E.G. SCHIZOPHRENIA DISORDERS).

Addenda -

Include Diagnosis too.

4. LIST ALL SOURCES OF FUNDING OR SPONSORSHIP OF THE WORK WHICH LED TO THE INVENTION.

A. Federal Sponsorship  $\phi$

(1) Federal Grant # \_\_\_\_\_ McLean Fund # \_\_\_\_\_

Principal Investigator \_\_\_\_\_

Title of Research Project: \_\_\_\_\_

(2) Federal Grant # \_\_\_\_\_ McLean Fund # \_\_\_\_\_

Principal Investigator \_\_\_\_\_

Title of Research Project: \_\_\_\_\_

B. Private Sponsorship  $\phi$

(1) Sponsor \_\_\_\_\_ McLean Fund # \_\_\_\_\_

Principal Investigator \_\_\_\_\_

Title of Research Project: \_\_\_\_\_

(2) Sponsor \_\_\_\_\_ McLean Fund # \_\_\_\_\_

Principal Investigator \_\_\_\_\_

Title of Research Project: \_\_\_\_\_

C. Other Sponsorship  $\phi$

(1) \_\_\_\_\_

(2) \_\_\_\_\_

5. HISTORY OF THE INVENTION.

A. When did you first think of (conceive) the invention?

Date \_\_\_\_\_

B. When did you first disclose your invention to another person?

Date \_\_\_\_\_ To Whom JIM RUSCHKE Affiliation REFUGEN

C. When was the first written description or drawing of your invention produced? (Please attach photocopy of such written description.)

Date \_\_\_\_\_

6. DISCLOSURE. In order to obtain valid patent protection in this country, a patent application must be filed with the United States Patent and Trademark Office within one year after the invention is first described in a printed publication anywhere

*in the world and within one year after the invention is first on sale or in public use in the United States. To preserve patent rights in many foreign countries, a United States patent application must be filed before any public disclosure in any form anywhere in the world and an application must be filed in the foreign country within one year from the U.S. filing date. If these deadlines are not met, the invention is deemed no longer "new" for patent purposes, and therefore not patentable. Dates which can result in a patent bar include, for example, the first public use of the invention, the publication date of a journal article, the mailing date of an abstract of an oral presentation, the date of any presentation (oral or written) at a professional seminar, etc.*

**A. Journals.** *Include all manuscripts describing the invention that have been published, accepted for publication but not yet published, and submitted pending acceptance.*

- (1) Name of Journal φ  
Title of Manuscript \_\_\_\_\_  
Author(s) \_\_\_\_\_  
(Anticipated) Date of submission \_\_\_\_\_ Date of Acceptance \_\_\_\_\_  
(Anticipated) Date of publication \_\_\_\_\_ Volume and page number \_\_\_\_\_
- (2) Name of Journal φ  
Title of Manuscript \_\_\_\_\_  
Author(s) \_\_\_\_\_  
(Anticipated) Date of submission \_\_\_\_\_ Date of Acceptance \_\_\_\_\_  
(Anticipated) Date of publication \_\_\_\_\_ Volume and page number \_\_\_\_\_

**B. Conferences.** *Include conferences at which any presentation concerning the invention has been made, as well as conferences which have not yet occurred but for which a manuscript or abstract has been submitted. Also include any conferences at which you intend to disclose information concerning the invention within the next six months. In that case, give the best information that you have at the present time.*

- (1) Title of Conference φ  
Date \_\_\_\_\_ Location \_\_\_\_\_  
Title of abstract or manuscript submitted \_\_\_\_\_  
Was the abstract or manuscript distributed prior to the conference? \_\_\_\_\_ If so, when? \_\_\_\_\_
- (2) Title of Conference φ  
Date \_\_\_\_\_ Location \_\_\_\_\_  
Title of abstract or manuscript submitted \_\_\_\_\_  
Was the abstract or manuscript distributed prior to the conference? \_\_\_\_\_ If so, when? \_\_\_\_\_

**C. Offer for sale or public use.**

- (1) Has this invention been offered for sale? φ If so, When? \_\_\_\_\_  
To whom and under what circumstances? \_\_\_\_\_  
\_\_\_\_\_
- (2) Has this invention been used publicly? \_\_\_\_\_ If so, When? \_\_\_\_\_  
To whom and under what circumstances? \_\_\_\_\_  
\_\_\_\_\_

D. Other. 0

Have you or any co-inventor listed above signed a confidentiality or secrecy agreement in exchange for receiving any proprietary information from a third party pertaining to the research which gave rise to the invention? \_\_\_\_\_

If so, when? \_\_\_\_\_

To whom and under what circumstances? \_\_\_\_\_

6. INVENTOR(S) SIGNATURE(S):

DATE

Perry J. Neum  
Clara d. Hughes-Todd

WITNESS(ES): Disclosed to and understood by me on:

DATE

SIGNATURE

[Signature]

Please return completed form to:

Peter A. Paskevich, M.A.

Vice President

Director, Research Administration

McLean Hospital